Serum transaminase elevation in Patients with rotavirus gastroenteritis

Rotavirüs gastroenteritli çocuk hastalarda serum transaminaz düzeylerinde artış

Rotavirus and serum transaminase elevation

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Öz

Amaç: Bu çalışmayı yapmaktaki amacımız rotavirüs akut gastroenteriti ile ortalama indiare skoru arasında ilişkiyi değerlendirmektir. Gereç ve Yöntem: Ocak-Temmuz 2016 tarihleri arasında gastroenterit tanısı alan ve hidrasyon amacıyla hastaneye yatırılan 1 ay-16 yaş arası çocuk hastalar çalışmaya alındı. Rotavirüs pozitif gastroenteriti olan hastalar RPGE, rotavirus negatif gastroenteriti olan hastalar RNGE ve basit cerrahi prosedür için çocuk cerrahisi servisine yatırılan hastalar ise kontrol grubu olarak değerlendirildi. Bulgular: RPGE grubundaki hastaların AST ve ALT ortalamaları, RNGE ve kontrol gruplarının ortalamalarından daha yüksek bulundu(p:0.001; p<0.05). RPGE grubundaki olguların 21'inde (%52.5) sadece AST yüksekliği görülürken, 7'sinde (%17.5) hem AST hem de ALT yüksekliği vardı. RNGE grubundaki olguların ise 9'unda (%15) sadece AST yüksekliği görülürken, 4'ünde (%6.7) hem AST hem de ALT yüksekliği bir arada idi. RPGE ve RNGE grubundaki hastaların CRP ve WBC değerleri, kontrol gruplarındaki hastaların değerlerinden daha yüksek bulundu (p<0.05). RPGE ve RNGE grupları arasında anlamlı bir farklılık yoktu (p>0.05). Gruplar arasında PCT, MPV ve PLT değerleri açısından istatistiksel olarak anlamlı bir farklılık bulunmadı (p>0.05). RPGE grubundaki hastaların skor ortalamaları, RNGE grubunun ortalamalarından daha yüksekti ve bu yükseklik istatistiksel olarak anlamlıydı (p:0.001; p<0.05). Gastroenterit skor düzeyi ile PLT, AST ve ALT düzeyleri arasında pozitif yönlü ve anlamlı bir ilişki bulundu (p<0.05). Tartışma: Bu çalışma ile rotavirüs gastroenteritlerinin serum transaminaz artışı ile ilişkili olduğunu saptadık ve transaminaz yüksekliği olan akut gastroenteritli çocuk hastalarda rotavirüs enfeksiyonun hatırlanması gerektiğini vurgulamak istedik.

Anahtar Kelimeler

Rotavirüs; Gastroenterit; Aspartat Aminotransferaz; Alanin Aminotransferaz

Abstract

Aim: In the present study we aimed to assess the relationship between rotavirus gastroenteritis and mean platelet volume, serum alanine aminotransferase, aspartate aminotransferase, and diarrhea score. Material and Method: This study enrolled pediatric patients aged one month to 16 years who were diagnosed with gastroenteritis and hospitalized for rehydration between January 2016 and July 2016. Patients who had rotavirus positive gastroenteritis were grouped as RPGE group, and those with rotavirus negative gastroenteritis were grouped as RNGE group. Subjects who were hospitalized at pediatric surgery unit for simple surgical procedures were grouped as the control group. Results: Mean AST and ALT levels of the RPGE group were significantly greater than those of the RNGE group (p:0.001; p<0.05). Twenty-one (52.5%) patients in the RPGE group had AST elevation alone while 7 (17.5%) had elevation in both ALT and AST. In the RNGE group, 9 (15%) patients had AST elevation alone, and 4 (6.7%) had elevations in both ALT and AST. The RPGE and RNGE groups had significantly greater CRP and WBC levels compared to the control group (p<0.05). RPGE and RNGE groups had no statistically significant difference in either parameter (p>0.05). There were no significant differences between the groups regarding PCT, MPV, and PLT levels (p>0.05). The mean diarrhea score of the RPGE group were significantly greater than those of the RNGE group (p:0.001; p<0.05). A significant positive correlation was found between the gastroenteritis score and PLT, AST, and ALT levels (p<0.05). Discussion: By means of the present study we determined that rotavirus gastroenteritis was correlated to elevated serum transaminase levels. We would like to stress that rotavirus infection should be remembered in children with acute gastroenteritis and elevated transaminases.

Keywords

Rotavirus; Gastroenteritis; Aspartate Aminotransferase; Alanine Aminotransferase

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Introduction

Infectious gastroenteritides are the most common cause of mortality and morbidity after lower respiratory infections in children. Rotavirus gastroenteritis is associated with 2-3 million hospitalizations and 600.000 deaths especially in developing countries each year among children aged less than 5 years. Nosocomial rotavirus gastroenteritis is known to prolong hospital stay and to increase cost [1].

Rotavirus infection stimulates humoral and cell-mediated immune response at mucosal level, and the virus is normally cleared by one week. However, it may persist as severe chronic diarrhea associated with rotavirus excretion. The symptoms rapidly emerge after an incubation period of 1-2 day. Dehydration, which appears as a major complication, emerges shortly after disease onset and has a variable severity. Symptoms usually persist for 5-7 days. Death usually takes place due to dehydration, metabolic disturbances, and shock. Rotavirus infections may also cause viremia and other systemic disorders such as pancreatitis, cerebellitis, systemic inflammatory response syndrome, disseminated intravascular coagulation, toxic megacolon, encephalopathy, and biliary atresia. Extraintestinal manifestations are also reported, but their reasons are unknown [2,3].

Various studies have shown that the percentage of children with laboratory signs of hepatitis, defined as increased serum ALT levels, varies from 15% to 37%, and it is not clear whether this occurs due to a potential hepatotropism, or induction of proinflammatory cytokines caused by viral infection, resulting in hepatocyte necrosis [4-6].

Thrombocytes play important roles in the pathogeneses of diseases associated with local or systemic inflammation. Large platelets are known as stress platelets, and increased MPV is associated with increased megakaryocyte growth as a response to thrombopoietic stress. Diseases with increased production of young platelets are also accompanied by macro thrombocytosis in association with increased destruction and sudden release of newly produced cells. Young platelets are large, dense, and more active [7,8]. While MPV was defined as a positive acute phase reactant in some of the previously reported studies, it was designated as a negative acute phase reactant in some others [9].

The first aim of the present study was to study ALT, AST, and MPV levels in patients with rotavirus positive acute gastroenteritis and to compare them with corresponding levels obtained from the RNGE and CG groups. Its second aim was to seek a relationship between rotavirus acute gastroenteritis MPV, AST, ALT levels and the diarrhea score.

Material and Methods

This study was approved by Gaziantep University Ethics Committee (2015, 81). It involved pediatric patients aged one month to 16 years who were admitted to the emergency department and department of pediatrics to receive rehydration therapy between January 2016 and June 2016. Patients with rotavirus detected in stool examination were grouped as the rotavirus positive acute gastroenteritis (RPGE) group and those with no detectable rotavirus in their stools as rotavirus negative acute gastroenteritis (RNGE). The control group consisted of patients without chronic disorders admitted to the pediatric surgery department for minor surgical procedures.

Patients with missing medical information, chronic disorders, malnutrition, obesity, malabsorption syndromes, idiopathic thrombocytopenic purpura, thrombocyte function disorders, thrombosis, malignancy, and hypersplenism were excluded, as were those who were older than 17 years, who underwent thrombocyte transfusion, who had bleeding throughout the study, who had immune deficiency, who were taking aspirin, heparin, chemotherapy, hepatotoxic therapy, or non-steroid immunosuppressive therapy.

The recorded parameters included age, sex, diarrhea score, complete blood count parameters [white blood cell count, absolute neutrophil count (ANC), platelet count, mean platelet volume (MPV), serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), blood urea nitrogen (BUN), creatinine, and C reactive protein (CRP)].

Complete blood counts were studied within 1 hour with Abbott CellDyn® 3700 system (Abbott Diagnostics, Santa Clara, CA, USA) using blood samples anticoagulated with K3 EDTA.

Rotavirus was detected in stool samples using the ELISA method (Rota Antigen Test Device, Cambridge) which has a sensitivity of 86-98% and a specificity of 92-96%.

Serum biochemistry samples were studied using a standard biochemical analyzer (Hitachi 902 Automatic Analyzer, Roche Diagnostics, Germany). Normal ALT values were defined as 13-40 IU/L and normal AST values were defined as 10-45 IU/L. Diarrhea scoring was done using the Vesikari scoring system in which fever, vomiting, and diarrhea duration and severity were scored.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics 22 (IBM SPSS, Türkiye) software package. Shapiro Wilk test was used to check if study data were normally distributed. Descriptive statistics included mean, standard deviation, frequency. Quantitative variables with normal distribution were compared with Oneway ANOVA test with Tukey HDS posthoc analysis. Non-normally distributed parameters were compared using Kruskal Wallis test, and the pairs with a significant difference in the analyzed parameter were determined with Mann Whitney U test. Qualitative parameters were compared using Chi-square test. Correlation between normally distributed variables was tested with Pearson correlation analysis, and the correlation between non-normally distributed variables was tested with Spearman's rho correlation analysis. A p value of less than 0.05 was considered statistically significant.

Results

One hundred and sixty patients enrolled in the study had a mean age of 45.72±43.15(minimum 2-max 174) months; 55 (34.4%) were female, and 105 (65.6%) were male. There were 40 patients in the RPGE group, 60 patients in the RNGE group, and 60 patients in the control group. There were no significant differences between the study groups concerning mean age and sex distribution (p>0.05). The demographic properties and laboratory results of the study groups were shown in Table 1. A significant difference existed between mean AST levels (p:0.001;

Table 1. The comparison of the demographic properties and laboratory results of the study groups

	RPGE	RNGE	Control	p
	Ort±SS	Ort±SS	Ort±SS	
Age (months)	38,38±33,4	51,17±45,84	45,17±45,94	[1]0,348
Sex n, %				
Female	12 (%30)	20 (%33,3)	23 (%38,3)	[3]0,675
Male	28 (%70)	40 (%66,7)	37 (%61,7)	
Score	8,73±1,97	7,28±1,53	-	[2]0,001*
CRP(mg/dL)	1,82±5,24	1,27±2,14	0,12±0,27	[2]0,001*
WBC(/mm^3)	10,74±5,43	11,54±4,64	8,46±2,44	[1]0,001*
ANS (/mm^3)	5,63±5,39	6,95±4,55	3,17±1,49	[2]0,001*
MPV(fL)	7,06±1,21	7,12±0,93	6,9±0,82	[1]0,458
PLT(/mm^3)	327,3±96,94	326,43±96,21	357,63±112,55	[1]0,188
AST(U/L)	54,1±35,69	35,9±12,21	33±10,68	[1]0,001*
ALT (U/L)	37,63±35,06	22,4±18,19	18,02±8,36	[2]0,001*
PCT(ng/mL)	0,19±0,17	0,29±0,32	2±0	[2]0,201

[1]Oneway Anova test [2]Kruskal Wallis test [3]Chi-square test
*p<0.05
CRP:C-reactive protein, WBC:White blood cell, ANS:Absolute neutrophil count, MPV:Mean platelet volume, PLT:Platelet count, AST:Aspartate aminotransferase, ALT:Alanine aminotransferase, PCT:Procalcitonin

Table 2. Correlation analysis between the diarrhea score and laboratory parameters

		Score		
		Total	RPGE	RNGE
[1]CRP	r	-0,118	0,044	-0,189
	p	0,242	0,787	0,148
[2]WBC	r	0,194	0,462	0,025
	p	0,054	0,003*	0,851
[1]ANS	r	-0,017	0,088	0,088
	p	0,864	0,589	0,502
[2]MPV	r	-0,051	-0,155	0,079
	p	0,617	0,339	0,547
[2]PLT	r	0,269	0,285	0,297
	p	0,007*	0,075	0,021*
[2]AST	r	0,256	0,141	0,183
	p	0,010*	0,387	0,162
[2]ALT	r	0,443	0,451	0,276
	p	0,001*	0,004*	0,033*

[1]Oneway Anova test [2]Kruskal Wallis test [3]Chi-square test
*p<0.05
CRP:C-reactive protein, WBC:White blood cell, ANS:Absolute neutrophil count, MPV:Mean platelet volume, PLT:Platelet count, AST:Aspartate aminotransferase, ALT:Alanine aminotransferase, PCT:Procalcitonin

p<0.05). The mean AST level of the RPGE group was significantly greater than those of the RNGE and control groups (p:0.001; p<0.05). No significant difference existed between RNGE and control groups (p>0.05).

There were significant differences between the mean ALT levels of the study groups (p:0.001; p<0.05). Patients in the RPGE group had a significantly greater mean ALT level compared to those of the RNGE and control groups (p:0.001; p<0.05). However, RNGE and control groups were not significantly different (p>0.05).

Twenty-one (52.5%) patients in the RPGE group had AST elevation alone while 7 (17.5%) had both AST and ALT elevation. In the RNGE group, on the other hand, 9 (15%) had AST elevation alone while 4 (6.7%) had both AST and ALT elevation.

The mean scores of the RPGE group were significantly greater than those of the RNGE group (p:0.001; p<0.05).

CRP and WBC levels of the RPGE and RNGE groups were significantly greater than those of the control group (p<0.05). There was no significant difference between the RPGE and RNGE groups (p>0.05).

The mean ANS of the RNGE group was significantly greater than that of RPGE (p:0.040) and the control groups (p:0.001). RPGE group also had a significantly greater mean ANS than the controls (p:0.044; p<0.05). No significant differences were found between the groups about PCT, MPV and PLT levels (p>0.05). The diarrhea score had a significant positive correlation with PLT, AST and ALT levels (p<0.05) (Table 2).

Discussion

This study demonstrated that rotavirus gastroenteritides are associated with transaminase elevation. This elevation in transaminases may reflect intestinal and muscle injury. While AST is found in liver, brain, and skeletal muscle, ALT is localized in the liver. The observed transaminase abnormalities may either reflect liver injury caused by the virus per se or they may stem from an immunological response or the production and release of a metabolite or toxin during the infection.

Akelma et al. reported that 15.4% of children with rotavirus positive acute gastroenteritis had ALT elevation and 25.4% had AST elevation, while the corresponding figures for rotavirus negative acute gastroenteritis were 6.8% and 11.9%, respectively (p<0.001) [10]. The authors stressed that transaminase elevation returned to normal in both groups during follow-up and that rotavirus should be considered in the differential diagnosis of acute gastroenteritis whenever transaminase elevation is detected. Similarly, in a study dated 2007 where 92 RPGE cases were studied, ALT and AST elevation were present in 20% of the cases [11]. Kawashima et al. reported that 85% of cases with rotavirus gastroenteritis had elevated AST level and 11.5% had elevated ALT level, and that they found a correlation between elevated AST and IL-6 level [12]. They also reported that rotavirus infection is mostly associated with mild hepatitis, which was not correlated to neurological complications. Our study also indicated AST elevation alone in 52.5% of the RPGE cases and elevation of both AST and ALT in 17.5% of the same group. In the RNGE group, on the other hand, 15% of the patients had AST elevation alone while 6.7% of the same group showed elevation in both AST and ALT levels. Detection of transaminase abnormalities in a certain, albeit lower, percentage of patients with rotavirus negative gastroenteritis suggests that other causes of viral gastroenteritis may also lead to hepatic transaminase elevation.

In a study dated 2017 involving 619 children, rotavirus positivity, and gastroenteritis severity were independent risk factors for both ALT and AST elevation [13]. We determined a significant positive correlation between the gastroenteritis score and AST and ALT levels (p<0.05).

Therefore, variations in platelet volume markers are of prophylactic and diagnostic importance in thrombotic and prethrombotic events. Various studies have shown an increase in MPV in acute coronary syndrome, diabetes mellitus, cerebrovascu-

lar events, renal artery stenosis, hypercholesterolemia, familial Mediterranean fever, and sepsis [14]. A decrease in MPV has been shown to be correlated with disease activity in ulcerative colitis and Crohn's disease. Erhan et al. reported higher MPV in patients with inflammatory bowel disease compared with controls [9]. Some studies in recent years have reported that MPV values did not increase in all situations of inflammation. Kısacık et al. found MPV to be lower during active periods of rheumatoid arthritis and ankylosing spondylitis compared with the control group [15].

Çelik et al. in a study on 151 patients with rotavirus gastroenteritis, found MPV levels of 7.47 fL and 7.79 fL in the RPGE and control group, respectively (p:0.000) [16]. Gastroenteritis score was positively correlated with leucocyte count, PLT count, and CRP but not to MPV. Based on these findings, the authors concluded that MPV could be used as an acute phase reactant in children with rotavirus gastroenteritis. In a study dated 2013, Mete et al. found MPV levels of 7.35, 7.30, and 7.80 fL in the RPGE, RNGE, and control groups, respectively (p<0.0001) [17]. In contrast, we determined MPV levels of 7.06, 7.12, and 6.9 fL in the RPGE, RNGE, and control groups, respectively, and found no significant differences between the groups (p:0.458). In accordance with the literature, we also found a significant positive correlation between the gastroenteritis score and PLT count. We failed to detect any significant correlation between MPV and the gastroenteritis score.

Our study demonstrated significantly greater CRP level and WBC count in the RPGE and RNGE groups compared with the controls (p<0.05). We considered that this might have developed secondary to inflammation associated with gastroenteritis.

By means of this study, we determined an association between rotavirus gastroenteritis and transaminase elevation, and we aimed to stress that rotavirus infection should be considered in the differential diagnosis in children with acute gastroenteritis. We concluded that MPV level was not a useful marker for diagnosing rotavirus gastroenteritis.

Animal and Human Rights

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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Competing interests

The authors declare that they have no competing interests.

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